```
=> d que l10
L1          3662 SEA (VANADOCENE# OR ((VANAD? OR OXOVANAD?) (2A) ACETYLACETONAT?
                 ))
L3        433888 SEA ANTIANGIOGEN? OR ANGIOGEN? OR RESTENOSIS OR HYPERPLAS? OR
                 PROLIFERAT? DISORDER# OR NEOVASCULAR? OR RETINOPATH? OR
                 HEMANGIOMA#
L4           543 SEA L1 (L) L3
L5             3 SEA L1 (100A) L3
L6           540 SEA L4 NOT L5
L7            18 SEA (L1 (250A) L3) AND L6
L9           522 SEA L4 NOT (L5 OR L7)
L10          522 DUP REM L9 (0 DUPLICATES REMOVED)

=> d que 12; d que 18
L2        388096 SEA ANTIANGIOGEN? OR ANGIOGEN? OR RESTENOSIS OR HYPERPLAS? OR
                 PROLIFERAT? DISORDER# OR NEOVASCULAR? OR RETINOPATY? OR
                 HEMANGIOMA#


L1          3662 SEA (VANADOCENE# OR ((VANAD? OR OXOVANAD?) (2A) ACETYLACETONAT?
                 ))
L3        433888 SEA ANTIANGIOGEN? OR ANGIOGEN? OR RESTENOSIS OR HYPERPLAS? OR
                 PROLIFERAT? DISORDER# OR NEOVASCULAR? OR RETINOPATH? OR
                 HEMANGIOMA#
L4           543 SEA L1 (L) L3
L5             3 SEA L1 (100A) L3
L6           540 SEA L4 NOT L5
L7            18 SEA (L1 (250A) L3) AND L6
L8             0 SEA FILE=STNGUIDE L4 NOT (L5 OR L7)

=> d que 112
L1          3662 SEA (VANADOCENE# OR ((VANAD? OR OXOVANAD?) (2A) ACETYLACETONAT?
                 ))
L3        433888 SEA ANTIANGIOGEN? OR ANGIOGEN? OR RESTENOSIS OR HYPERPLAS? OR
                 PROLIFERAT? DISORDER# OR NEOVASCULAR? OR RETINOPATH? OR
                 HEMANGIOMA#
L4           543 SEA L1 (L) L3
L5             3 SEA L1 (100A) L3
L6           540 SEA L4 NOT L5
L7            18 SEA (L1 (250A) L3) AND L6
L9           522 SEA L4 NOT (L5 OR L7)
L10          522 DUP REM L9 (0 DUPLICATES REMOVED)
L11       119140 SEA VANAD?/TI,AB,CLM
L12           15 SEA L10 AND L11
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L5, L7, L12 reviewed online

FILES
Caplus
WPIDS
Medline
Embase
PCTfull
Europatfull
Uspatfull

FILE 'CAPLUS, WPIDS, MEDLINE, EMBASE, CANCERLIT' ENTERED AT 19:54:34 ON 24 JUN 2002

L7	41	S VANAD? AND (ANGIOGENESIS OR ANGIOGENETIC OR ANTIANGIOGENESIS)
L8	24	DUP REM L7 (17 DUPLICATES REMOVED)
L9	1	S L8 AND VANADOCENE
L10	23	S L8 NOT L9

See also L13 + L14 (Done later with diff./alternative terms)

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FILE 'CAPLUS' ENTERED AT 20:44:17 ON 24 JUN 2002
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FILE 'WPIDS' ENTERED AT 20:44:17 ON 24 JUN 2002
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FILE 'MEDLINE' ENTERED AT 20:44:17 ON 24 JUN 2002

FILE 'EMBASE' ENTERED AT 20:44:17 ON 24 JUN 2002
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FILE 'CANCERLIT' ENTERED AT 20:44:17 ON 24 JUN 2002

=> s (vanad? and (neovascular? or angiogenic or antiangiogenic)) not l7
L13          17 (VANAD? AND (NEOVASCULAR? OR ANGIOGENIC OR ANTIANGIOGENIC)) NOT
                L7

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14           9 DUP REM L13 (8 DUPLICATES REMOVED)
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=> d l9 all; d l10 1-23 bib hit

L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
AN 2001:275687 CAPLUS
DN 135:220738
TI X-ray structure, solution properties, and biological activity profile of **vanadocene**(IV) acetylacetonate complex, [VCp2(acac)](CF3SO3): a dual-function anti-cancer agent with anti-angiogenic and anti-mitotic properties
AU Ghosh, P.; Ghosh, S.; Navara, C.; Narla, R. K.; Benyumov, A.; Uckun, F. M.
CS Department of Chemistry, Parker Hughes Institute, Parker Hughes Cancer Center, St. Paul, MN, 55113, USA
SO Journal of Inorganic Biochemistry (2001), 84(3-4), 241-253
CODEN: JIBIDJ; ISSN: 0162-0134
PB Elsevier Science Inc.
DT Journal
LA English
CC 1-6 (Pharmacology)
Section cross-reference(s): 78
AB The structure of [V(.eta.5-C5H5)2(CH3C(O)CHC(O)CH3)](O3SCF3) (1) (=[VCp2(acac)](O3SCF3)), a dual-function anti-cancer agent with anti-angiogenic and anti-mitotic properties, was detd. by single-crystal X-ray diffraction. The geometry is well described as a pseudo-tetrahedral like structure with the centroids of the cyclopentadienyl rings and the two oxygen atoms of the acetylacetonate ring in the ancillary positions of the central **vanadium** (IV) atom. The bisector of the V(acac) fragment deviates from the C2 axis of the ligand framework by only 4.degree., compared to a deviation of 7.degree. for the V(acac) fragment in the tetramethylethano-bridged **vanadocene** acetyl acetonate complex. Crystal data for 1: space group, P21/c; a=7.5544(9) A, b=14.936(2) A, c=16.193(2) A, .beta.=102.901(2).degree., V=1781.0(4) A3; Z=4; R=0.0506 for 2310 reflections with I>2.sigma.(I). This report also details the ESR, UV/Vis spectroscopy, electrochem. properties and the biol. activity profile of this potent anti-cancer agent.
ST antitumor **vanadocene** acetylacetonate complex crystal structure
IT Mitosis
(inhibitors; properties and biol. activity of antitumor **vanadocene**(IV) acetylacetonate complex)
IT **Angiogenesis** inhibitors
Antitumor agents
Crystal structure
Cyclic voltammetry
ESR (electron spin resonance)
Stability
UV and visible spectra
(properties and biol. activity of antitumor **vanadocene**(IV) acetylacetonate complex)
IT 208989-61-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(properties and biol. activity of antitumor **vanadocene**(IV) acetylacetonate complex)
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L10 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2002 ACS
AN 2001:137014 CAPLUS
DN 134:173061
TI Peroxovanadium compounds as protein tyrosine phosphatase (PTP) inhibitors, their inhibitory effects on **angiogenesis**, restenosis and the production of endothelins, and their stimulating effects on the immune response
IN Batistini, Bruno Joseph; Doillon, Charles; Faure, Robert; Olivier, Martin; Posner, Barry; Savard, Pierre
PA Universite Laval, Can.
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001012180	A2	20010222	WO 2000-CA898	20000803
	WO 2001012180	A3	20010816		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	EP 1202728	A2	20020508	EP 2000-952813	20000803

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRAI	CA 1999-2280249	A	19990812
	WO 2000-CA898	W	20000803

TI Peroxovanadium compounds as protein tyrosine phosphatase (PTP) inhibitors, their inhibitory effects on **angiogenesis**, restenosis and the production of endothelins, and their stimulating effects on the immune response

AB The invention relates to the use of peroxovanadium compds. in the prevention of **angiogenesis**, restenosis and the prodn. of endothelins, and as immunomodulators. Peroxovanadium compds. are preferred since they are more potent, and less toxic, than their "oxo" counterparts. Anti-angiogenic activity was verified in vitro against human umbilical vascular endothelial cells (HUVECs) as well as ex ovo using the chicken chorioallantoic assay membrane and in the rat aortic ring model and a Matrigel assay in vivo. Peroxovanadium compds. also decrease basal levels and inhibit the increase in plasma endothelins occurring following insulin induction in rats. It is proposed that peroxovanadium compds. are therapeutically active anti-angiogenics and useful in preventing vascular restenosis by acting, inter alia, by inhibiting one or several protein tyrosine phosphatases involved in the proliferation, differentiation, and migration of cells or the secretion of peptides (e.g. endothelins and immunomodulators), or both.

ST peroxovanadium compd protein tyrosine phosphatase inhibitor; **angiogenesis** inhibitor restenosis immunomodulator peroxovanadium compd; endothelin prodn peroxovanadium compd

IT Animal cell line
Cell differentiation
(HUVEC; peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT Leishmania
Pathogen
(adjuvant for vaccination against; peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT Vaccines
(adjuvant for; peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT Immunostimulants
(adjuvants; peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis

and prodn. of endothelins, and immunostimulant effects)

IT Artery
(angioplasty; peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT mRNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cytokine; peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT Gene
(expression, chemokine; peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interferon-inducible IP-10; peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT **Angiogenesis** inhibitors
Anti-inflammatory agents
Eosinophil
Immunostimulants
Leishmania major
Leukocyte
Macrophage
Neutrophil
(peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT Chemokines
Cytokines
Interleukin 10
Interleukin 12
Interleukin 1.alpha.
Interleukin 1.beta.
Interleukin 2
Interleukin 4
Interleukin 6
Macrophage inflammatory protein 1.alpha.
Macrophage inflammatory protein 1.beta.
Macrophage inflammatory protein 2
Monocyte chemoattractant protein-1
RANTES (chemokine)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT Artery, disease
(restenosis; peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT Interferons
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.gamma.; peroxovanadium compds. as protein tyrosine phosphatase

inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT 7439-98-7D, Molybdenum, peroxo compds., biological studies 7440-03-1D, Niobium, peroxo compds., biological studies 7440-25-7D, Tantalum, peroxo compds., biological studies 7440-32-6D, Titanium, peroxo compds., biological studies 7440-33-7D, Tungsten, peroxo compds., biological studies 7440-62-2D, **Vanadium**, peroxo compds., biological studies 68782-50-3 68832-77-9 68832-78-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

IT 10102-43-9, Nitric oxide, biological studies 79747-53-8, Protein tyrosine phosphatase 116243-73-3, Endothelin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peroxovanadium compds. as protein tyrosine phosphatase inhibitors, inhibitory effects on **angiogenesis**, restenosis and prodn. of endothelins, and immunostimulant effects)

L10 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2002 ACS
AN 2000:861683 CAPLUS
DN 134:29250
TI Bacteriochlorins and bacteriopurpurins useful as photoselective compounds for photodynamic therapy and a process for their production
IN Robinson, Byron C.
PA Miravant Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000073308	A2	20001207	WO 2000-US13999	20000523
	WO 2000073308	A3	20010419		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6376483	B1	20020423	US 1999-320731	19990527
	EP 1189906	A2	20020327	EP 2000-936158	20000523
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1999-320731	A	19990527		
	WO 2000-US13999	W	20000523		

OS MARPAT 134:29250
IT **Angiogenesis**
(neovascularization, retinal; prepn. of bacteriochlorins and bacteriopurpurins useful as photoselective compds. for photodynamic therapy)
IT 7429-90-5DP, Aluminum, diformyl and bis(acrylate) porphyrin deriv.

complexes, preparation 7429-91-6DP, Dysprosium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7439-89-6DP, Iron, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7439-91-0DP, Lanthanum, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7439-92-1DP, Lead, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7439-94-3DP, Lutetium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7439-96-5DP, Manganese, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7439-98-7DP, Molybdenum, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-00-8DP, Neodymium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-02-0DP, Nickel, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-05-3DP, Palladium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-06-4DP, Platinum, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-10-0DP, Praseodymium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-16-6DP, Rhodium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-19-9DP, Samarium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-20-2DP, Scandium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-22-4DP, Silver, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-27-9DP, Terbium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-28-0DP, Thallium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-29-1DP, Thorium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-30-4DP, Thulium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-31-5DP, Tin, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-32-6DP, Titanium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-36-0DP, Antimony, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-45-1DP, Cerium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-47-3DP, Chromium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-48-4DP, Cobalt, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-50-8DP, Copper, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-52-0DP, Erbium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-53-1DP, Europium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-54-2DP, Gadolinium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-58-6DP, Hafnium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-60-0DP, Holmium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-61-1DP, Uranium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-62-2DP, **Vanadium**, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-64-4DP, Ytterbium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-65-5DP, Yttrium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-66-6DP, Zinc, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-67-7DP, Zirconium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation 7440-74-6DP, Indium, diformyl and bis(acrylate) porphyrin deriv. complexes, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reactant for prepn. of bacteriochlorins and bacteriopurpurins useful as photoselective compds. for photodynamic therapy)

L10 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2002 ACS
AN 2000:53434 CAPLUS
DN 132:106961

TI Cancer treatment methods using therapeutic conjugates that bind to aminophospholipids
IN Thorpe, Philip E.; Ran, Sophia
PA Board of Regents, the University of Texas System, USA
SO PCT Int. Appl., 266 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000002587	A1	20000120	WO 1999-US15668	19990712
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9950958	A1	20000201	AU 1999-50958	19990712
	BR 9912053	A	20010403	BR 1999-12053	19990712
	EP 1098665	A1	20010516	EP 1999-935491	19990712
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6312694	B1	20011106	US 1999-351457	19990712
PRAI	US 1998-92589P	P	19980713		
	US 1998-110600P	P	19981202		
	WO 1999-US15668	W	19990712		

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Angiogenesis** inhibitors
Antitumor agents
Chemotherapy
Crosslinking agents
Cytotoxic agents
DNA sequences
Drug targeting
Drugs
Hybridoma
Neoplasm
Protein sequences
Test kits
Vipera russelli
X-ray
(anti-aminophospholipid antibody conjugates with diagnostic or therapeutic agent for targeting tumor blood vessels)

IT 7429-91-6D, Dysprosium, trivalent and conjugate, biological studies
7439-89-6D, Iron, divalent or trivalent and conjugate, biological studies
7439-91-0D, Lanthanum, trivalent and conjugate, biological studies
7439-92-1D, Lead, divalent and conjugate, biological studies 7439-96-5D, Manganese, divalent and conjugate, biological studies 7440-00-8D, Neodymium, trivalent and conjugate, biological studies 7440-02-0D, Nickel, divalent and conjugate, biological studies 7440-19-9D, Samarium, trivalent and conjugate, biological studies 7440-27-9D, Terbium, trivalent and conjugate, biological studies 7440-47-3D, Chromium, trivalent and conjugate, biological studies 7440-48-4D, Cobalt, divalent and conjugate, biological studies 7440-50-8D, Copper, divalent and

conjugate, biological studies 7440-52-0D, Erbium, trivalent and conjugate, biological studies 7440-54-2D, Gadolinium, trivalent and conjugate, biological studies 7440-57-5D, Gold, trivalent and conjugate, biological studies 7440-60-0D, Holmium, trivalent and conjugate, biological studies 7440-62-2D, **Vanadium**, divalent and conjugate, biological studies 7440-64-4D, Ytterbium, trivalent and conjugate, biological studies 7440-69-9D, Bismuth, divalent and conjugate, biological studies 9001-99-4D, Ribonuclease, conjugate 9002-04-4D, Blood-coagulation factor IIa, conjugate 9002-05-5D, Blood coagulation factor Xa, conjugate 9035-58-9D, Blood-coagulation factor III, polymeric or derivs and conjugate 10043-66-0D, Iodine-131, conjugate, biological studies 10098-91-6D, Yttrium-90, conjugate, biological studies 13981-51-6D, Mercury-197, conjugate, biological studies 13982-78-0D, Mercury-203, conjugate, biological studies 14119-09-6D, Gallium-67, conjugate, biological studies 14133-76-7D, Technetium-99, conjugate, biological studies 14158-31-7D, Iodine-125, conjugate, biological studies 14378-26-8D, Rhenium-188, conjugate, biological studies 14885-78-0D, Indium-113, conjugate, biological studies 14998-63-1D, Rhenium-186, conjugate, biological studies 15715-08-9D, Iodine-123, conjugate, biological studies 15750-15-9D, Indium-111, conjugate, biological studies 15757-14-9D, Gallium-68, conjugate, biological studies 15757-86-5D, Copper-67, conjugate, biological studies 20830-81-3D, Daunorubicin, conjugate 22438-27-3D, Rubidium-103, conjugate, biological studies 22453-63-0D, Rubidium-97, conjugate, biological studies 23214-92-8D, Doxorubicin, conjugate 25316-40-9D, Adriamycin, conjugate 37270-94-3D, Platelet factor 4, conjugate 37316-87-3D, Blood coagulation Factor IXa, conjugate 57576-52-0D, Thromboxane A2, conjugate 60832-04-4D, Thromboxane A2 synthase, conjugate 62031-54-3D, Fibroblastic growth factor, conjugate 65312-43-8D, Blood-coagulation factor VIIa, conjugate 86102-31-0D, TIMP, conjugate 127464-60-2D, Vascular endothelial growth factor, conjugate 138757-15-0D, .alpha.2-Antiplasmin, conjugate
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-aminophospholipid antibody conjugates with diagnostic or therapeutic agent for targeting tumor blood vessels)

L10 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2002 ACS
AN 2000:53432 CAPLUS
DN 132:106960
TI Cancer treatment methods using antibodies to aminophospholipids
IN Thorpe, Philip E.; Ran, Sophia
PA Board of Regents, the University of Texas System, USA
SO PCT Int. Appl., 226 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000002584	A2	20000120	WO 1999-US15600	19990712
	WO 2000002584	A3	20000330		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	AU 9954585	A1	20000201	AU 1999-54585	19990712
	EP 1096955	A2	20010509	EP 1999-940802	19990712
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6406693	B1	20020618	US 1999-351543	19990712
PRAI	US 1998-92672P	P	19980713		
	US 1998-110608P	P	19981202		
	WO 1999-US15600	W	19990712		

IT **Angiogenesis** inhibitors
Antitumor agents
Chemotherapy
Coagulants
Cytotoxic agents
DNA sequences
Drug delivery systems
Hybridoma
Neoplasm
Phage display library
Protein sequences
Test kits
(anti-aminophospholipid antibody conjugate for targeting diagnostic and therapeutic agent to tumor blood vessel endothelium)

IT 7429-91-6D, Dysprosium, trivalent isotope and conjugate, biological studies 7439-89-6D, Iron, di- and trivalent isotope and conjugate, biological studies 7439-91-0D, Lanthanum, trivalent and conjugate, biological studies 7439-92-1D, Lead, divalent and conjugate, biological studies 7439-96-5D, Manganese, divalent isotope and conjugate, biological studies 7440-00-8D, Neodymium, trivalent isotope and conjugate, biological studies 7440-02-0D, Nickel, divalent isotope and conjugate, biological studies 7440-19-9D, Samarium, trivalent isotope and conjugate, biological studies 7440-27-9D, Terbium, trivalent isotope and conjugate, biological studies 7440-47-3D, Chromium, trivalent isotope and conjugate, biological studies 7440-48-4D, Cobalt, divalent isotope and conjugate, biological studies 7440-50-8D, Copper, divalent isotope and conjugate, biological studies 7440-52-0D, Erbium, trivalent isotope and conjugate, biological studies 7440-54-2D, Gadolinium, trivalent isotope and conjugate, biological studies 7440-57-5D, Gold, trivalent and conjugate, biological studies 7440-60-0D, Holmium, trivalent isotope and conjugate, biological studies 7440-62-2D, **Vanadium**, divalent isotope and conjugate, biological studies 7440-64-4D, Ytterbium, trivalent isotope and conjugate, biological studies 7440-69-9D, Bismuth, trivalent and conjugate, biological studies 10043-66-0D, Iodine-131, conjugate, biological studies 10098-91-6D, Yttrium-90, conjugate, biological studies 13981-51-6D, Mercury-197, conjugate, biological studies 13982-78-0D, Mercury-203, conjugate, biological studies 14119-09-6D, Gallium-67, conjugate, biological studies 14133-76-7D, Technetium-99, conjugate, biological studies 14158-31-7D, Iodine-125, conjugate, biological studies 14378-26-8D, Rhenium-188, conjugate, biological studies 14885-78-0D, Indium-113, conjugate, biological studies 14998-63-1D, Rhenium-186, conjugate, biological studies 15715-08-9D, Iodine-123, conjugate, biological studies 15750-15-9D, Indium-111, conjugate, biological studies 15757-14-9D, Gallium-68, conjugate, biological studies 15757-86-5D, Copper-67, conjugate, biological studies 22438-27-3D, Rubidium-103, conjugate, biological studies 22453-63-0D, Rubidium-97, conjugate, biological studies 37270-94-3D, Platelet factor 4, conjugate 62031-54-3D, FGF, conjugate 86102-31-0D, TIMP, conjugate 127464-60-2D,

Vascular endothelial growth factor, conjugate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-aminophospholipid antibody conjugate for targeting diagnostic and therapeutic agent to tumor blood vessel endothelium)

L10 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2002 ACS
AN 1999:783929 CAPLUS
DN 132:18780
TI Compositions comprising antimicrotubule agents for treating or preventing inflammatory diseases
IN Hunter, William L.
PA Angiotech Pharmaceuticals, Inc., Can.
SO PCT Int. Appl., 340 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962510	A2	19991209	WO 1999-CA464	19990601
	WO 9962510	A3	20000406		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9940255	A1	19991220	AU 1999-40255	19990601
PRAI	US 1998-88546P	P	19980601		
	US 1998-88546	A	19980601		
	WO 1999-CA464	W	19990601		

IT Adhesion, biological
Angiogenesis inhibitors
Anti-inflammatory agents
Antiarthritics
Antitumor agents
Astrocyte
Cytotoxic agents
Drug delivery systems
Micelles
Microtubule
Neutrophil
Permeation enhancers
Psoriasis
Transplant rejection
(antimicrotubule agents for treating or preventing inflammatory diseases)

IT 50-04-4 52-21-1 57-22-7 59-05-2 64-86-8 145-63-1 446-72-0 865-21-4, Vincaleukoblastine 7689-03-4 9050-30-0D, fragments 10540-29-1 27774-13-6 37353-31-4, **Vanadate** 38213-69-3 52205-73-9 63177-57-1 66107-60-6 77699-47-9, Herbimycin 86102-31-0 100827-28-9 144676-04-0 174882-69-0, Pycnogenol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antimicrotubule agents for treating or preventing inflammatory diseases)

L10 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2002 ACS
AN 1999:764062 CAPLUS
DN 132:10375
TI Agents interfering with the binding of protein tyrosine phosphatase PEST to domains of signaling proteins as inhibitors of cell migration and/or of focal adhesion
IN Tremblay, Michel L.; Cote, Jean-Francois; Angers-Lousteau, Alexandre; Charest, Alain
PA McGill University, Can.
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9961467	A2	19991202	WO 1999-CA461	19990521
	WO 9961467	A3	20000518		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2329157	AA	19991202	CA 1999-2329157	19990521
	AU 9939229	A1	19991213	AU 1999-39229	19990521
	EP 1077997	A2	20010228	EP 1999-922004	19990521
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002516338	T2	20020604	JP 2000-550871	19990521
	WO 2000036111	A1	20000622	WO 1999-CA1184	19991210
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1137780	A1	20011004	EP 1999-957819	19991210
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI	CA 1998-2238654	A	19980521
	US 1998-111993P	P	19981211
	WO 1999-CA461	W	19990521
	WO 1999-CA1184	W	19991210

AB This invention relates to agents or compds. capable of interfering with the binding of protein tyrosine phosphatase PEST to protein domains of signaling mols. involved in cell migration, focal adhesion and/or cell proliferation, namely p130cas and paxillin. The agents can be derived from the minimal sequences found in binding studies. PTP-PEST is a conserved phosphatase essential for embryo development. Knock-out cells (PTP-PEST -/-) have been perpetuated from null embryos and they show defects in cell migration, focal adhesion and cell proliferation.

Therefore, any agent capable of interfering with the activity of PEST in a diseased target tissue, is considered to be a potential therapeutic agent to treat any disease having any of the following etiol. components: cell proliferation, cancer, metastasis, inflammation, and **angiogenesis** . This invention further relates to a method for finding genuine substrates for enzymes, namely phosphatases, combining gene targeting knock-out technique and substrate-trapping technique with the aid of a substrate binding inactive mutant enzyme. By using a gene targeting knock-out technique, there are less artifacts than by using other techniques (using **vanadate** compds., for example) wherein an artificial non-specific increase of the level of hyperphosphorylation occurs. Gene targeting of the PTP-PEST suppresses fibroblast motility on the extracellular matrix fibronectin as shown in wound-healing migration assays. Hyperphosphorylation of actin cytoskeleton protein PSTPIP in PEST -/- cells affected the cleavage of furrow formation. This was the first demonstration that the p130cas family of proteins, HefI and Sin interact in a similar manner with a proline rich region found on PTP-PEST with their SH3 domains. It was also shown that PTP-PEST binds to paxillin through its PRO2 region. LIM domains 3 and 4 of paxillin were required for PTP-PEST binding. The design of peptides interfering with the binding of a phosphatase to a signaling protein derived from binding studies is shown.

ST tyrosine phosphatase PEST signal transduction migration focal adhesion; cancer therapy **angiogenesis** wound healing PEST phosphatase

IT **Angiogenesis**
Antitumor agents
Cell proliferation
Inflammation
(methods for treatment of; agents interfering with binding of protein tyrosine phosphatase PEST to domains of signaling proteins)

L10 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2002 ACS
AN 1999:37955 CAPLUS
DN 130:192300
TI Expression of the AT2 receptor developmentally programs extracellular signal-regulated kinase activity and influences fetal vascular growth
AU Akishita, Masahiro; Ito, Masaaki; Lehtonen, Jukka Y. A.; Daviet, Laurent; Dzau, Victor J.; Horiuchi, Masatsugu
CS Cardiovascular Research, Department of Medicine, Harvard Medical School, Brigham and Women's Hospital, Boston, MA, 02115, USA
SO Journal of Clinical Investigation (1999), 103(1), 63-71
CODEN: JCINAO; ISSN: 0021-9738
PB American Society for Clinical Investigation
DT Journal
LA English
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Angiotensin II type 2 (AT2) receptor is abundantly expressed in vascular smooth muscle cells (VSMC) of the fetal vasculature during late gestation (embryonic day 15-20), during which the blood vessels undergo remodeling. To examine directly the influence of AT2 receptor expression in the developmental biol. of VSMC, we studied cultures of VSMC from fetal and postnatal wild-type (Agtr2+) and AT2 receptor null (Agtr2-) mice. Consistent with in vivo data, AT2 receptor binding in cultured Agtr2+ VSMC increased by age, peaking at embryonic day 20, and decreased dramatically after birth. Angiotensin II-induced growth in Agtr2+ VSMC (embryonic day 20) was increased by the AT2 receptor blocker PD123319, indicating that the AT2 receptors are functional and exert an antigrowth effect in Agtr2+ VSMC. Growth of VSMC in response to serum decreased age dependently and

was higher in Agtr2- than in Agtr2+, inversely correlating with AT2 receptor expression. However, serum-induced growth in Agtr2+ and Agtr2- VSMC and the exaggerated Agtr2- VSMC growth was maintained even in the presence of PD123319 or losartan, an AT1 receptor blocker. Moreover, Agtr2- VSMC showed greater growth responses to platelet-derived growth factor and basic fibroblast growth factor, indicating that Agtr2- cells exhibit a generalized exaggerated growth phenotype. We studied the mechanism responsible for this phenotype and obsd. that extracellular signal-regulated kinase (ERK) activity was higher in Agtr2- VSMC at baseline and also in response to serum. ERK kinase inhibitor PD 98059 inhibited both growth and ERK phosphorylation dose-dependently, while the regression lines between growth and ERK phosphorylation were identical in Agtr2+ and Agtr2- VSMC, suggesting that increased ERK activity in Agtr2- VSMC is pivotal in the growth enhancement. Furthermore, the difference in ERK phosphorylation between Agtr2+ and Agtr2- was abolished by **vanadate** but not by okadaic acid, implicating tyrosine phosphatase in the difference in ERK activity. These results suggest that the AT2 receptor expression during the fetal vasculogenesis influences the growth phenotype of VSMC via the modulation of ERK cascade.

IT **Angiogenesis**
Blood vessel
Cell proliferation
Development, mammalian postnatal
Signal transduction, biological
(angiotensin AT2 receptor expression developmentally programs extracellular signal-regulated kinase activity and influences fetal vascular growth and signaling therein)

L10 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2002 ACS
AN 1997:313638 CAPLUS
DN 127:28712
TI Thrombospondin 1 and type I repeat peptides of thrombospondin 1 specifically induce apoptosis of endothelial cells
AU Guo, Neng-Hua; Krutzsch, Henry C.; Inman, John K.; Roberts, David D.
CS Laboratory of Pathology, National Cancer Institute NIH, Bethesda, MD, 20892-1500, USA
SO Cancer Research (1997), 57(9), 1735-1742
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Thrombospondin 1 (TSP1) inhibits **angiogenesis** and modulates endothelial cell adhesion, motility, and growth. The antiproliferative activity of TSP1 is mimicked by synthetic peptides derived from the type I repeats of TSP1 that antagonize fibroblast growth factor 2 and activate latent transforming growth factor .beta.. These TSP1 analogs induced programmed cell death in bovine aortic endothelial cells based on morphol. changes, assessment of DNA fragmentation, and internucleosomal DNA cleavage. Intact TSP1 also induced DNA fragmentation. The endothelial cell response was specific because no DNA fragmentation was induced in MDA-MB-435S breast carcinoma cells, although TSP1 and the peptide conjugates inhibited the growth of both cell types. Apoptosis did not depend on activation of latent transforming growth factor .beta. because peptides lacking the activating sequence RFK were active. Apoptosis was not sensitive to inhibitors of ceramide generation but was inhibited by the phosphatase inhibitor **vanadate**. Induction of DNA fragmentation by the peptides was decreased when endothelial cell cultures reached confluence. Growth of the cells on a fibronectin substrate also suppressed induction of apoptosis by TSP1 or the peptides. Differential

sensitivities to kinase inhibitors suggest that apoptosis and inhibition of proliferation are mediated by distinct signal transduction pathways. These results demonstrate that induction of apoptosis by the TSP1 analogs is not a general cytotoxic effect and is conditional on a lack of strong survival-promoting signals, such as those provided by a fibronectin matrix. The antitumor activity of TSP1 may therefore result from an increased sensitivity to apoptosis in endothelial cells adjacent to a provisional matrix during formation of vascular beds in tumors expressing TSP1.

ST antitumor thrombospondin endothelium **angiogenesis** apoptosis

IT **Angiogenesis** inhibitors
Antitumor agents
Apoptosis
(thrombospondin 1 and type I repeat peptides of thrombospondin 1 specifically induce apoptosis of endothelial cells)

L10 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2002 ACS
AN 1992:646041 CAPLUS
DN 117:246041
TI Involvement of prostanoids in the regulation of **angiogenesis** by polypeptide growth factors
AU Spisni, E.; Manica, F.; Tomasi, V.
CS Dep. Exp. Biol., Univ. Bologna, Bologna, 40126, Italy
SO Prostaglandins, Leukotrienes Essent. Fatty Acids (1992), 47(2), 111-15
CODEN: PLEAEU; ISSN: 0952-3278
DT Journal
LA English
TI Involvement of prostanoids in the regulation of **angiogenesis** by polypeptide growth factors
AB Polypeptide growth factors (PGFs), mainly those of the FGF family, have been shown to be capable of regulating **angiogenesis**. Although many data have been accumulated during this last year on the mechanism of action of PGF, little is known about a possible identification of second messengers signalling to the cell of occupancy of the receptor by its ligand. It was previously proposed that arachidonic acid or its derivs. may play a role as PGF second messengers. The present paper describes a modification of the chorioallantoic membrane (CAM) technique, involving the use of labeled sulfate to follow the angiogenic process in chick embryos. Thus, morphol. observation of CAMs development were correlated with the incorporation of labeled sulfate. As expected, PGF as endothelial cell growth factor (ECGS) or basic FGF potentiate the incorporation of radioactivity into CAMs at concns. which for bFGF are of the order of 1.5 .mu.g/egg. This effect can be correlated to the generation of prostanoids by 2 approaches: PGE1 injected into eggs strongly increased the labeling of CAMs; and indomethacin had a dramatic effect on embryo survival as well as on CAM development, decreasing both at very low concn. (50% survival rate at 2 .mu.g/egg). Finally **vanadate**, which is known to inhibit tyrosine phosphatase, potentiated the effect of PGF on **angiogenesis**. Evidently, products of the prostaglandin H synthase pathway behave as mediators of PGF control of **angiogenesis**.

ST prostaglandin growth factor **angiogenesis** embryo

IT Prostaglandins
RL: BIOL (Biological study)
(**angiogenesis** stimulation by peptide growth factors mediation by)

IT Animal growth regulators
RL: BIOL (Biological study)
(**angiogenesis** stimulation by, prostanoids involvement in)

IT Animal growth regulators
RL: BIOL (Biological study)
(endothelial cell growth factors, **angiogenesis** stimulation by, prostanoids involvement in)
IT 745-65-3, PGE1
RL: BIOL (Biological study)
(**angiogenesis** stimulation by peptide growth factors potentiation by)
IT 59763-19-8, Prostaglandin H synthase
RL: BIOL (Biological study)
(**angiogenesis** stimulation by peptide growth factors regulation by)
IT 106096-93-9, Basic fibroblast growth factor
RL: BIOL (Biological study)
(**angiogenesis** stimulation by, prostanoids involvement in)

L10 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2002 ACS
AN 1988:184290 CAPLUS
DN 108:184290
TI Induction of **angiogenesis** in vitro by **vanadate**, an inhibitor of phosphotyrosine phosphatases
AU Montesano, R.; Pepper, M. S.; Belin, D.; Vassalli, J. D.; Orci, L.
CS Med. Cent., Univ. Geneva, Geneva, 1211, Switz.
SO J. Cell. Physiol. (1988), 134(3), 460-6
CODEN: JCLLAX; ISSN: 0021-9541
DT Journal
LA English
TI Induction of **angiogenesis** in vitro by **vanadate**, an inhibitor of phosphotyrosine phosphatases
AB It has previously been shown that capillary endothelial cells grown on the surface of 3-dimensional collagen gels can be induced to invade the underlying fibrillar matrix and to form capillary-like tubular structures in response to tumor-promoting phorbol esters or the angiogenic agent fibroblast growth factor (FGF). Since both phorbol esters and FGF stimulate phosphorylation of tyrosine residues, endothelial cells were treated with **vanadate**, an inhibitor of phosphotyrosine-specific phosphatases, to det. whether this agent could induce the expression of an angiogenic phenotype in these cells. **Vanadate** stimulated endothelial cells to invade collagen matrixes and to organize into characteristic tubules resembling those induced by FGF or phorbol esters. **Vanadate** also concomitantly stimulated endothelial cells to produce plasminogen activators (PAs), proteolytic enzymes which are induced by phorbol esters and FGF and which have been implicated in the neovascular response; this stimulation could be accounted for by an increase in the levels of urokinase-type PA and tissue-type PA mRNA. These results suggest a role for tyrosine phosphorylation in the regulation of the angiogenic phenotype in capillary endothelial cells.
ST **angiogenesis** phosphotyrosine phosphatase; capillary formation phosphotyrosine phosphatase
IT Phosphorylation, biological
(of tyrosine, in **angiogenesis** regulation)
IT Ribonucleic acids, messenger
RL: BIOL (Biological study)
(tissue-type plasminogen activator-specifying, of capillary vessel endothelial cells, phosphotyrosine phosphatase in **angiogenesis** regulation in relation to)
IT Ribonucleic acids, messenger
RL: BIOL (Biological study)
(urokinase-type plasminogen activator-specifying, of capillary vessel

endothelial cells, phosphotyrosine phosphatase in **angiogenesis** regulation in relation to)

IT 16561-29-8, 4.beta.-Phorbol 12-myristate 13-acetate 106096-93-9, Basic fibroblast growth factor
RL: BIOL (Biological study)
(**angiogenesis** induction by, phosphotyrosine phosphatase in relation to)

IT 79747-53-8, Phosphotyrosinephosphatase
RL: BIOL (Biological study)
(in **angiogenesis** regulation)

IT 60-18-4, Tyrosine, biological studies
RL: BIOL (Biological study)
(phosphorylation of, in **angiogenesis** regulation)

IT 105913-11-9, Plasminogen activator
RL: BIOL (Biological study)
(tissue- and urokinase-type, formation of, by capillary endothelial cells, phosphotyrosine phosphatase in **angiogenesis** regulation in relation to)

L10 ANSWER 11 OF 23 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-303977 [34] WPIDS
DNC C2002-088378
TI New 5-amino-3-substituted-pyrazole (4,5-d)thiazole compounds are cyclic-dependent kinase inhibitors, useful for treating e.g. cancer, diabetic retinopathy and immunological disorders.
DC B02 B03
IN CHONG, W K M; DUVADIE, R K
PA (CHON-I) CHONG W K M; (DUVA-I) DUVADIE R K; (AGOU-N) AGOURON PHARM INC
CYC 96
PI WO 2002012250 A2 20020214 (200234)* EN 53p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
US 2002049215 A1 20020425 (200235)
ADT WO 2002012250 A2 WO 2001-US41466 20010731; US 2002049215 A1 Provisional US 2000-223989P 20000809, US 2001-923432 20010808
PRAI US 2000-223989P 20000809; US 2001-923432 20010808
AB WO 200212250 A UPAB: 20020528
NOVELTY - 5-Amino-3-substituted-pyrazole (4,5-d)thiazole compounds (I) are new.

DETAILED DESCRIPTION - 5-Amino-3-substituted-pyrazole (4,5-d)thiazole compounds of formula (I) and their salts, multimeric forms, prodrugs, metabolites and metabolite salts are new.

R1, R2 = alkyl, (hetero)aryl or (hetero)cycloalkyl (all optionally substituted);

provided that both R1 and R2 may not be substituted phenyl.

ACTIVITY - Cytostatic; Antidiabetic; Ophthalmological; Antirheumatic; Antiarthritic; Vasotropic; Antipsoriatic.

MECHANISM OF ACTION - CDK4 or CDK4/cyclin Complex Inhibitor; Protein Kinase Activator; Protein Kinase Receptor Modulator or Inhibitor, CDK4 and/or CDK2 Inhibitor.

An assay was performed in 96 well plates (50 ml) in the presence of N-(2-hydroxyethyl)piperazine-N'(2-ethane sulfonic acid) (HEPES) (10 mM), MgCl2 (10 mM), adenosine triphosphate (ATP)(25 micro M), ovalbumin (1 mg/ml), leupeptin (5 micro g/ml), dithiothreitol (1 mM), glycerophosphate (10 mM), sodium **vanadate** (0.1 mM), sodium fluoride (1 mM),

ethylene glycol-bis(beta -aminotethylether)-N,N,N',N'-tetraacetic acid (EDTA) (2.5 mM), dimethyl sulfoxide (2 vol.%); and Ci(32/33P) ATP (0.03-0.4 mM) per reaction. 3-Phenyl-5-(4-sulfonamidophenyl-amino) -1H-pyrazolo (4,5-d)thiazole hydrobromic acid salt displayed a ki value of 34 nM for purified CDK2/A. was .

USE - (I) Are useful in the preparation of a pharmaceutical composition for treating a disease or disorder mediated by inhibition of CDK4 or CDK4/cyclin complex, protein kinase activity e.g. associated with tumor growth, cell proliferation or **angiogenesis** in a mammal (all claimed); for treating malignancies or cancers and disease associated with unwanted mycotic infection. The diseases associated with cellular proliferation are diabetic retinopathy, glaucoma, rheumatoid arthritis, restenosis and psoriasis, immunological disorders involving undesired proliferation of leukocytes and other smooth muscle disorders.

ADVANTAGE - (I) Effectively block the transition of cancer cells into their proliferative phase.

Dwg.0/0

L10 ANSWER 12 OF 23 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-106298 [14] WPIDS
DNC C2002-032662
TI New matrix metalloproteinase inhibitor useful for treating for e.g. cancer, **angiogenesis**, arthritis, connective tissue disease, cardiovascular disease, inflammation and autoimmune disease.
DC B03 K08
IN FRIDMAN, R; MOBASHERY, S
PA (FRID-I) FRIDMAN R; (MOBA-I) MOBASHERY S; (UYWA-N) UNIV WAYNE STATE
CYC 22
PI WO 2001092244 A1 20011206 (200214)* EN 59p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU JP US
AU 2001065182 A 20011211 (200225)
US 2002037916 A1 20020328 (200225)
ADT WO 2001092244 A1 WO 2001-US17448 20010530; AU 2001065182 A AU 2001-65182 20010530; US 2002037916 A1 Provisional US 2000-207874P 20000530, Provisional US 2000-226858P 20000822, US 2001-870403 20011003
FDT AU 2001065182 A Based on WO 200192244
PRAI US 2000-226858P 20000822; US 2000-207874P 20000530; US 2001-870403 20011003
TI New matrix metalloproteinase inhibitor useful for treating for e.g. cancer, **angiogenesis**, arthritis, connective tissue disease, cardiovascular disease, inflammation and autoimmune disease.
AB WO 200192244 A UPAB: 20020301
NOVELTY - Compounds (I) which are matrix metalloproteinase inhibitors, and their salts are new.

DETAILED DESCRIPTION - Compounds of formula (I), which are matrix metalloproteinase inhibitors, and their salts are new.

A-X-M = hydrophobic group;

D = O, S, 1-6C alkyl, a direct bond, SO2, SO, C(=O)NR, C(=O)O, NRC(=O) or OC(=O);

E = direct bond, 1-6C alkyl, 3-8C cycloalkyl, 2-6C alkenyl or 2-6C alkynyl (where (cyclo)alkyl, alkenyl or alkynyl is optionally substituted with at least one 1-6C alkyl, hydroxy, 1-6C alkoxy, cyano, nitro, halo, SR, NRR or COOR);

R = H or 1-6C alkyl;

J = S or O; and

G, T and Q = H, cyano or 1-6C alkyl.

INDEPENDENT CLAIMS are included for the following:

(1) a radiolabeled compound comprising (I) and a radionuclide; and

(2) a method of inhibiting a matrix metalloproteinase (preferably gelatinase) comprising a zinc atom involving contacting the matrix metalloproteinase with a compound containing a group (preferably thiirane ring) that can be activated for nucleophilic substitution by the zinc atom and can form a covalent bond with a nucleophile of the matrix metalloproteinase.

ACTIVITY - Cytostatic; Antiarthritic; Cardiant; Antiinflammatory; Immunosuppressive; Contraceptive.

MECHANISM OF ACTION - Matrix metalloproteinase (MMP) such as gelatinase (preferably MMP-2 or MMP-9), collagenase, stromelysin, membrane-type MMP or matrilysin inhibitor.

The inhibition activity of 4-phenoxyphenylsulfonylmethyl thiirane (Ia) against MMP-2 and MMP-9 was tested according to Olson, M.W.; Gervasi, D.C.; Mobashery, S.; Fridman, R. J.Biol. Chem. 1997,272,29975-29983. The onset inhibition (kon)(M-1S-1) multiply 10-4 for MMP-2/MMP-9 was 11 plus or minus 1/1.4 plus or minus 0.3; the recovery of activity from inhibition (koff) (1S-1) multiply 103 for MMP-2/MMP-9 was 1.5 plus or minus 0.6/9 plus or minus 1 and the inhibition constant (ki)(micro M) for MMP-2/MMP-9 was 0.0139 plus or minus 0.0004/0.6 plus or minus 0.2.

USE - In medical therapy or diagnosis; in the manufacture of a medicament useful for treating or preventing cancer, **angiogenesis**, arthritis, connective tissue disease, cardiovascular disease, inflammation and autoimmune disease in mammals; for inhibiting matrix metalloproteinase (MMP) (preferably gelatinase), for imaging tumor in mammals by administering (I) and then detecting presence of the compound e.g. in humans and mammalian tissue with MMP-activity, for preventing ovulation in mammals and for preventing the implantation of a fertilized egg into the uterus of mammals (all claimed).

ADVANTAGE - The inhibitor exhibits selectivity for at least one specific MMPs than known competitive inhibitors. The inhibitor do not showed negative long-term side effects.

Dwg.0/3

TECH UPTX: 20020301

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: No general preparation of (I) is given.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Radionuclide: The radionuclide is a non-metallic radionuclide (preferably fluorine-19, carbon-11, fluorine-18, iodine-123 or bromine-76). (I) comprises a chelating group containing a detectable radionuclide. The detectable radionuclide is a metallic radionuclide (preferably Antimony-124, Antimony-125, Arsenic-74, Barium-103, Barium-140, Beryllium-7, Bismuth-206, Bismuth-207, Cadmium-109, Cadmium-115m, Calcium-45, Cerium-139, Cerium-141, Cerium-144, Cesium-137, Chromium-51, Cobalt-55, Cobalt-56, Cobalt-57, Cobalt-58, Cobalt-60, Cobalt-64, Copper-67, Erbium-169, Europium-152, Gallium-64, Gallium-68, Gadolinium-153, Gadolinium-157, Gold-195, Gold-199, Hafnium-175, Hafnium-175-181, Holmium-166, Indium-110, Indium-111, Iridium-192, Iron-55, Iron-59, Krypton-85, Lead-210, Manganese-54, Mercury-197, Mercury-203, Molybdenum-99, Neodymium-147, Neptunium-237, Nickel-63, Niobium-95, Osmium-185 + 191, Palladium-103, Platinum-195m, Praseodymium-143, Promethium-147, Protactinium-233, Radium-226, Rhenium-186, Rhenium-188, Rubidium-86, Ruthenium-103, Ruthenium-106, Scandium-44, Scandium-46, Selenium-75, Silver-110m, Silver-111, Sodium-22, Strontium-85, Strontium-89, Strontium-90, Sulfur-35, Tantalum-182, Technetium-99m, Tellurium-125, Tellurium-132, Thallium-204, Thorium-228, Thorium-232, Thallium-170, Tin-113, Tin-114, Tin-117m, Titanium-44, Tungsten-185, **Vanadium**-48, **Vanadium**-49, Ytterbium-169, Yttrium-86, Yttrium-88, Yttrium-90, Yttrium-91, Zinc-65, or Zirconium-95).

Preferred Method: In the inhibition method the compound is preferably of

formula (I) and comprises a second group (preferably SO2) that can form at least one H-bond with an electrophile of the matrix metalloproteinase. The contacting step in inhibition method is carried out in vivo or in vitro.

TT TT: NEW MATRIX INHIBIT USEFUL TREAT CANCER **ANGIOGENESIS** ARTHRITIS CONNECT TISSUE DISEASE CARDIOVASCULAR DISEASE INFLAMMATION DISEASE.

L10 ANSWER 13 OF 23 WPIDS (C) 2002 THOMSON DERWENT
AN 1998-052013 [05] WPIDS
CR 1995-263711 [34]
DNC C1998-017802
TI Treatment of mammals with arthropathy e.g. arthritis, or proliferation of synoviocytes - comprises systemic administration of **vanadium** compound (except bis(methyl-maltolato)oxovanadium), e.g. orthovanadate and sodium **vanadate**.
DC B05 B06
IN CRUZ, T
PA (MOUN) MOUNT SINAI HOSPITAL CORP
CYC 77
PI WO 9747296 A2 19971218 (199805)* EN 56p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU ZW
AU 9730209 A 19980107 (199820)
US 5871779 A 19990216 (199914)
ADT WO 9747296 A2 WO 1997-CA405 19970612; AU 9730209 A AU 1997-30209 19970612; US 5871779 A CIP of US 1994-181980 19940118, CIP of WO 1995-CA19 19950118, US 1996-662859 19960612
FDT AU 9730209 A Based on WO 9747296
PRAI US 1996-662859 19960612; US 1994-181980 19940118; WO 1995-CA19 19950118
TI Treatment of mammals with arthropathy e.g. arthritis, or proliferation of synoviocytes - comprises systemic administration of **vanadium** compound (except bis(methyl-maltolato)oxovanadium), e.g. orthovanadate and sodium **vanadate**.
AB WO 9747296 A UPAB: 19990412
Treatment of mammals with arthropathy comprises systemic administration of an amount of a **vanadium** compound (I) effective to reduce or inhibit the arthropathy, provided that (I) is not bis(methylmaltolato)oxovanadium (BMOV). Also claimed are: (1) a method for reducing proliferation of synoviocytes in mammals comprising administration of (I) as above; (2) pharmaceutical compositions for treatment of proliferative disorders comprising: (A) an amount of **vanadium** complex effective to reduce cell proliferation selected from: (i) metavanadate and orthovanadate complexes; (ii) organo-**vanadium** compounds where the **vanadium** is bound to an organic moiety that can form a 5-6-membered ring or to an organic moiety such as hydroxamate, alpha -hydroxypyridinone, alpha -hydroxypyrone, alpha -amino acid, hydroxycarbonyl or thiohydroxamate; and (iii) coordinate-covalent complexes of **vanadyl** and cysteine or its derivatives, **vanadyl** acetylacetonate or **vanadyl** sulphate; and (B) one or more of a pharmaceutically acceptable carrier, diluent or excipient; (3) use of a **vanadium** complex selected from (i)-(iii) to reduce cell proliferation and metalloprotease expression, reducing or inhibiting drug-resistant tumours and/or reducing metastasis.

USE - The methods are useful for treating arthopathies, e.g. inflammatory and degenerative diseases of the joints, particularly arthritis (claimed), rheumatoid arthritis, osteoarthritis, enteropathic arthritis, gouty arthritis, Jaccoud's arthritis and neuropathic arthritis, bone resorption, inflammatory disease, and CNS degenerative disorders; to promote wound healing, for treating cancers, e.g. leukaemias, lymphomas (Hodgkin's and non-Hodgkin's), sarcomas, melanomas, adenomas, solid tissue carcinomas, hypoxic tumours, squamous cell carcinomas of the mouth, throat, larynx, lung, breast, ovaries and colon, genitourinary cancers such as cervical and bladder cancer, haematopoietic cancers, human glioma and astrocytoma primary tumours, head and neck cancers, nervous system cancers, benign lesions such as papillomas, atherosclerosis, **angiogenesis** and viral infections, especially HIV infections; for treating drug resistance (e.g. resistance to multiple anticancer drugs such as colchicine, vinblastine and doxorubicin, or tumours expressing the multi-drug resistance proteins as described in R. Deeley et al., Science, 258:1650-1654,1992) and to reduce toxicity of other therapeutic agents. E.g. the composition may be used in combination with radiotherapy or chemotherapy, such as multi-drug chemotherapy for Hodgkins disease and chemotherapy treatment of breast cancer.

Dwg.0/8

TT TT: TREAT MAMMAL ARTHRITIS PROLIFERATION COMPRISE SYSTEMIC ADMINISTER **VANADIUM** COMPOUND DI METHYL ORTHOVANADATE SODIUM **VANADATE**.

L10 ANSWER 14 OF 23 WPIDS (C) 2002 THOMSON DERWENT
AN 1995-311860 [41] WPIDS
DNC C1995-138898
TI Treatment of proliferative disorders, metastases and drug resistant tumours - using **vanadate** cpds. opt. with antioxidants.
DC B05 B06
IN CRUZ, T
PA (MOUN) MOUNT SINAI HOSPITAL CORP
CYC 1
PI CA 2113683 A 19950719 (199541)* 47p
ADT CA 2113683 A CA 1994-2113683 19940118
PRAI CA 1994-2113683 19940118
TI Treatment of proliferative disorders, metastases and drug resistant tumours - using **vanadate** cpds. opt. with antioxidants.
AB CA 2113683 A UPAB: 19951019

Method for the treatment of proliferative disorders, comprises administering an amt. of **vanadate** cpd. (I) (including its derivs. or analogues), which result in a serum concn. of (I) of at least 5muM.

Admin. of (I) is also claimed for novel methods of (1) reducing or inhibiting the growth of drug resistant tumours; and (2) reducing metastases.

Pref. (I) is administered with at least one antioxidant (II) for treating proliferative disorders, drug resistant tumours or for reducing metastases (embodiment claimed).

Compsn. comprising (I) and a carrier, diluent or excipient, is also provided.

USE - (I) (opt. with (II)) reduce hydrogen peroxide to effect a redn. in cell proliferation and also reduce tumour metastases. Various forms of cancers (esp. haematopoietic tumours, human glioma and astrocytoma primary tumours), benign lesions, such as papillomas, atherosclerosis, **angiogenesis** and viral infections (esp. HIV infections), are specified for treatment. In addn. (I) may be used to treat drug resistant tumours (as claimed), e.g. tumours expressing high levels of

P-glycoprotein which is known to confer resistance to multiple anticancer drugs, such as colchicine, vinblastine, and doxorubicin.

Dosage is 0.2 (pref. 0.2-20) mg/kg. Dosage of N-acetylcysteine (IIa) is 40.0-1000 mg/kg, administered e.g. prior or during admin. of orthovanadate. The intracellular concn. of (I) is pref. 5-50muM. Dwg.0/18

TT TT: TREAT PROLIFERATION DISORDER METASTASIS DRUG RESISTANCE TUMOUR **VANADATE** COMPOUND OPTION ANTIOXIDANT.

L10 ANSWER 15 OF 23 MEDLINE

AN 2000150220 MEDLINE → abstract printed out on next page

DN 20150220 PubMed ID: 10684725

TI Restrictive endothelial barrier function during normal **angiogenesis** in vivo: partial dependence on tyrosine dephosphorylation of beta-catenin.

AU Cruz A; DeFouw L M; DeFouw D O

CS Department of Anatomy, UMDNJ-New Jersey Medical School, Newark, New Jersey 07103, USA.

NC GM17238 (NIGMS)
HL47936 (NHLBI)

SO MICROVASCULAR RESEARCH, (2000 Mar) 59 (2) 195-203.
Journal code: 0165035. ISSN: 0026-2862.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200005

ED Entered STN: 20000512
Last Updated on STN: 20000512
Entered Medline: 20000504

TI Restrictive endothelial barrier function during normal **angiogenesis** in vivo: partial dependence on tyrosine dephosphorylation of beta-catenin.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Allantois: BS, blood supply
Cadherins: PH, physiology
Capillary Permeability
Cell Differentiation
Chick Embryo
Chorion: BS, blood supply
*Cytoskeletal Proteins: ME, metabolism
Dextrans: PK, pharmacokinetics
Endothelium, Vascular: ME, metabolism
*Endothelium, Vascular: PH, physiology
Enzyme Inhibitors: PD, pharmacology
Fluorescein-5-isothiocyanate: AA, analogs & derivatives
Fluorescein-5-isothiocyanate: PK, pharmacokinetics
Fluorescent Dyes: PK, pharmacokinetics
*Neovascularization, Physiologic: PH, physiology
Phosphorylation
Phosphotyrosine: ME, metabolism
*Protein Processing, Post-Translational
Protein-Tyrosine-Phosphatase: AI, antagonists & inhibitors
*Protein-Tyrosine-Phosphatase: PH, physiology
Vanadates: PD, pharmacology

CN 0 (Cadherins); 0 (Cytoskeletal Proteins); 0 (Enzyme Inhibitors); 0 (Fluorescent Dyes); 0 (**Vanadates**); 0 (cadherin 5); 0 (fluorescein isothiocyanate dextran); 0 (pervanadate); EC 3.1.3.48 (Protein-Tyrosine-Phosphatase)

L10 15/23

AN **2000150220** MEDLINE
DN 20150220 PubMed ID: 10684725
TI Restrictive endothelial barrier function during normal angiogenesis in vivo: partial dependence on tyrosine dephosphorylation of beta-catenin.
AU Cruz A; DeFouw L M; DeFouw D O
CS Department of Anatomy, UMDNJ-New Jersey Medical School, Newark, New Jersey 07103, USA.
NC GM17238 (NIGMS)
HL47936 (NHLBI)
SO MICROVASCULAR RESEARCH, (2000 Mar) 59 (2) 195-203.
Journal code: 0165035. ISSN: 0026-2862.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200005
ED Entered STN: 20000512
Last Updated on STN: 20000512
Entered Medline: 20000504
AB Differentiation of a restrictive endothelial barrier in the chick chorioallantoic membrane (CAM) occurs between Day 4.5 and Day 5.0 of the normal 21-day gestation. Whether molecular changes in the endothelial cell-cell junctional protein complex contribute to the ontogeny of barrier function represents the principal focus of this study. VE-cadherin has been shown to contribute to the regulation of endothelial cell monolayer permeability in vitro. Accordingly, VE-cadherin is complexed to the cytosolic catenins, and changes in monolayer permeability have been linked to alterations of the cadherin/catenin complex. Currently, a CAM endothelial VE-cadherin/beta-catenin complex was identified, and phosphotyrosine labeling of beta-catenin was decreased concurrently with the abrupt increase in CAM endothelial selectivity between Day 4.5 and Day 5.0. Further, inhibition of protein tyrosine phosphatases impeded regular tyrosine dephosphorylation of beta-catenin at Day 5.0 and this served to partially restore macromolecular extravasation to elevated levels normally present at Day 4.5. Thus, differentiation of selective barrier function in the angiogenic CAM endothelium in vivo is dependent, in part, on tyrosine dephosphorylation of beta-catenin.

L10 ANSWER 16 OF 23 MEDLINE
AN 1999160432 MEDLINE
DN 99160432 PubMed ID: 10050071
TI Angiostatin diminishes activation of the mitogen-activated protein kinases ERK-1 and ERK-2 in human dermal microvascular endothelial cells.
AU Redlitz A; Daum G; Sage E H
CS Departments of Biological Structure and Surgery, University of Washington, Seattle, Wash., USA.
SO JOURNAL OF VASCULAR RESEARCH, (1999 Jan-Feb) 36 (1) 28-34.
Journal code: 9206092. ISSN: 1018-1172.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199904
ED Entered STN: 19990504
Last Updated on STN: 20000303
Entered Medline: 19990422
AB Angiostatin is an endogenous inhibitor of **angiogenesis** that was isolated from tumor-bearing mice. It has been established that angiostatin inhibits endothelial cell proliferation; however, the underlying mechanisms remain to be elucidated. Here we report that angiostatin reduces transiently the phosphorylation of the mitogen-activated protein kinases ERK-1 and ERK-2 in human dermal microvascular cells, but not in human vascular smooth muscle cells or human dermal fibroblasts. We demonstrate that angiostatin diminishes ERK activation by basic fibroblast growth factor and vascular endothelial growth factor. Dephosphorylation of ERK and other tyrosine-phosphorylated proteins was blocked by pretreatment of the cells with sodium meta-**vanadate**, an inhibitor of protein tyrosine phosphatases, indicating that angiostatin signaling may require the activity of a tyrosine phosphatase. Concentrations of angiostatin that inhibited ERK activation also inhibited basic fibroblast growth factor-stimulated collagen gel invasion by endothelial cells, but did not affect endothelial cell proliferation. We thus show that angiostatin inhibits primarily the invasion of endothelial cells and exerts minimal (if any) effects on their proliferation. Invasion is a process that involves proteolysis, adhesion and migration, all of which have been linked to ERK signaling.

L10 ANSWER 17 OF 23 MEDLINE
AN 97444374 MEDLINE
DN 97444374 PubMed ID: 9298995
TI Tyrosine residue in exon 14 of the cytoplasmic domain of platelet endothelial cell adhesion molecule-1 (PECAM-1/CD31) regulates ligand binding specificity.
AU Famiglietti J; Sun J; DeLisser H M; Albelda S M
CS Pulmonary and Critical Care Division, Department of Medicine, University of Pennsylvania Medical Center, Philadelphia, Pennsylvania 19104-4283, USA.
NC HL-03382 (NHLBI)
HL-46311 (NHLBI)
SO JOURNAL OF CELL BIOLOGY, (1997 Sep 22) 138 (6) 1425-35.
Journal code: 0375356. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710

ED Entered STN: 19971105
Last Updated on STN: 19971105
Entered Medline: 19971022

AB Platelet/endothelial cell adhesion molecule (PECAM-1) is a cell adhesion molecule of the immunoglobulin superfamily that plays a role in a number of vascular processes including leukocyte transmigration through endothelium. The presence of a specific 19- amino acid exon within the cytoplasmic domain of PECAM-1 regulates the binding specificity of the molecule; specifically, isoforms containing exon 14 mediate heterophilic cell-cell aggregation while those variants missing exon 14 mediate homophilic cell-cell aggregation. To more precisely identify the region of exon 14 responsible for ligand specificity, a series of deletion mutants were created in which smaller regions of exon 14 were removed. After transfection into L cells, they were tested for their ability to mediate aggregation. For heterophilic aggregation to occur, a conserved 5-amino acid region (VYSEI in the murine sequence or VYSEV in the human sequence) in the mid-portion of the exon was required. A final construct, in which this tyrosine was mutated into a phenylalanine, aggregated in a homophilic manner when transfected into L cells. Inhibition of phosphatase activity by exposure of cells expressing wild type or mutant forms of PECAM-1 to sodium orthovanadate resulted in high levels of cytoplasmic tyrosine phosphorylation and led to a switch from heterophilic to homophilic aggregation. Our data thus indicate either loss of this tyrosine from exon 14 or its phosphorylation results in a change in ligand specificity from heterophilic to homophilic binding. Vascular cells could thus determine whether PECAM-1 functions as a heterophilic or homophilic adhesion molecule by processes such as alternative splicing or by regulation of the balance between tyrosine phosphorylation or dephosphorylation. Defining the conditions under which these changes occur will be important in understanding the biology of PECAM-1 in transmigration, **angiogenesis**, development, and other processes in which this molecule plays a role.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Alternative Splicing: PH, physiology
*Antigens, CD31: CH, chemistry
*Antigens, CD31: GE, genetics
*Antigens, CD31: ME, metabolism
Binding Sites: PH, physiology
*Blood Platelets: CH, chemistry
Blood Platelets: ME, metabolism
Cytoplasm: CH, chemistry
*Exons: PH, physiology
Ligands
Mice
Mutagenesis: PH, physiology
Phosphorylation
Protein Binding: DE, drug effects
Protein Binding: GE, genetics
Protein Structure, Tertiary
Sensitivity and Specificity
Tyrosine: ME, metabolism
Vanadates: PD, pharmacology

CN 0 (Antigens, CD31); 0 (Ligands); 0 (**Vanadates**)

L10 ANSWER 18 OF 23 MEDLINE
AN 95076375 MEDLINE
DN 95076375 PubMed ID: 7527160
TI Postreceptor signal transduction mechanisms involved in octreotide-induced inhibition of **angiogenesis**.

AU Patel P C; Barrie R; Hill N; Landeck S; Kurozawa D; Woltering E A
CS Department of Surgery, Louisiana State University, New Orleans.
SO SURGERY, (1994 Dec) 116 (6) 1148-52.
Journal code: 0417347. ISSN: 0039-6060.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199501
ED Entered STN: 19950116
Last Updated on STN: 20000303
Entered Medline: 19950105
TI Postreceptor signal transduction mechanisms involved in octreotide-induced inhibition of **angiogenesis**.
AB BACKGROUND. Somatostatin analogues inhibit peptide release and cell growth through multiple postreceptor signal transduction mechanisms (PRSTM), including G proteins (GP), cyclic adenosine monophosphate (cAMP), calcium, protein kinase C (PKC), and tyrosine phosphatase (TP). Octreotide acetate (OA), a somatostatin analogue, has been shown to inhibit **angiogenesis**; however, the PRSTM involved are unknown. METHODS. Fertilized chicken eggs were obtained and incubated. On day 3, embryos were removed and placed in plastic wrap hammocks. On day 7, disks containing OA, test substances that interfere with PRSTM, or combinations of OA plus a test substance were placed on the developing chorioallantoic membrane. Blood vessel growth under each disk was assessed at 24 hours. Data were evaluated by chi-squared analysis. RESULTS. OA's ability to inhibit **angiogenesis** is significantly diminished when combined with calcium, bradykinin (increases calcium), pertussis toxin (inhibits GP), or 3-isobutyl-1-methylxanthine (increases cAMP). In contrast, no significant decrease is noted in OA's ability to inhibit **angiogenesis** when combined with phorbol ester (activates PKC) or **vanadate** (inhibits TP). CONCLUSIONS. OA-induced inhibition of **angiogenesis** is GP, calcium, and cAMP dependent and is PKC and TP independent. Better understanding of the PRSTM involved with OA-induced inhibition of **angiogenesis** may lead to enhancement of OA's effect on **angiogenesis**.

L10 ANSWER 19 OF 23 MEDLINE
AN 91283938 MEDLINE
DN 91283938 PubMed ID: 1711917
TI Proteolytic balance and capillary morphogenesis.
AU Pepper M S; Montesano R
CS Department of Morphology, University Medical Center, Geneva, Switzerland.
SO CELL DIFFERENTIATION AND DEVELOPMENT, (1990 Dec 2) 32 (3) 319-27. Ref: 30
Journal code: 8811335. ISSN: 0922-3371.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199108
ED Entered STN: 19910825
Last Updated on STN: 20000303
Entered Medline: 19910806
AB **Angiogenesis** is the process by which new capillary blood vessels are formed from preexisting vessels. A number of components of this morphogenetic process, including endothelial cell invasion and capillary lumen formation, are believed to be dependent on tightly controlled

proteolytic degradation of the extracellular matrix. The critical importance of an appropriate balance between proteases and protease inhibitors in these processes is suggested by two sets of observations. Firstly, that extracellular matrix invasion and capillary lumen formation are inhibited in the presence of an excess of protease inhibitors. Secondly, that when unchecked by protease inhibitors, excessive proteolysis is incompatible with normal capillary morphogenesis. These results clearly suggest that a precisely regulated proteolytic balance is necessary for normal capillary morphogenesis.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Aprotinin: PD, pharmacology
Capillaries: ME, metabolism
Cell Movement
*Endopeptidases: ME, metabolism
Endothelium, Vascular: CY, cytology
Endothelium, Vascular: ME, metabolism
Enzyme Induction
*Extracellular Matrix Proteins: ME, metabolism
Fibroblast Growth Factor 2: PH, physiology
Mice
Morphogenesis: DE, drug effects
*Neovascularization, Pathologic
Plasmin: ME, metabolism
Plasminogen Activators: BI, biosynthesis
*Protease Inhibitors: ME, metabolism
Tetradecanoylphorbol Acetate: PD, pharmacology
Transforming Growth Factor beta: PH, physiology
Urinary Plasminogen Activator: BI, biosynthesis
Vanadates: PD, pharmacology

CN 0 (Extracellular Matrix Proteins); 0 (Protease Inhibitors); 0 (Transforming Growth Factor beta); 0 (**Vanadates**); EC 3.4.- (Endopeptidases); EC 3.4.21.- (Plasminogen Activators); EC 3.4.21.7 (Plasmin); EC 3.4.21.73 (Urinary Plasminogen Activator)

L10 ANSWER 20 OF 23 MEDLINE
AN 90338128 MEDLINE
DN 90338128 PubMed ID: 1696269
TI Transforming growth factor-beta 1 modulates basic fibroblast growth factor-induced proteolytic and angiogenic properties of endothelial cells in vitro.
AU Pepper M S; Belin D; Montesano R; Orci L; Vassalli J D
CS Institute of Histology and Embryology, University of Geneva Medical Center, Switzerland.
SO JOURNAL OF CELL BIOLOGY, (1990 Aug) 111 (2) 743-55.
Journal code: 0375356. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X52906; GENBANK-X52907
EM 199009
ED Entered STN: 19901012
Last Updated on STN: 20000303
Entered Medline: 19900907
AB Tightly controlled proteolytic degradation of the extracellular matrix by invading microvascular endothelial cells is believed to be a necessary component of the angiogenic process. We have previously demonstrated the induction of plasminogen activators (PAs) in bovine microvascular endothelial (BME) cells by three agents that induce **angiogenesis**

in vitro: basic FGF (bFGF), PMA, and sodium orthovanadate. Surprisingly, we find that these agents also induce plasminogen activator inhibitor-1 (PAI-1) activity and mRNA in BME cells. We also find that transforming growth factor-beta 1 (TGF-beta 1), which in vitro modulates a number of endothelial cell functions relevant to **angiogenesis**, also increases both PAI-1 and urokinase-type PA (u-PA) mRNA. Thus, production of both proteases and protease inhibitors is increased by angiogenic agents and TGF-beta 1. However, the kinetics and amplitude of PAI-1 and u-PA mRNA induction by these agents are strikingly different. We have used the ratio of u-PA:PAI-1 mRNA levels as an indicator of proteolytic balance. This ratio is tilted towards enhanced proteolysis in response to bFGF, towards antiproteolysis in response to TGF-beta 1, and is similar to that in untreated cultures when the two agents are added simultaneously. Using an in vitro **angiogenesis** assay in three-dimensional fibrin gels, we find that TGF-beta 1 inhibits the bFGF-induced formation of tube-like structures, resulting in the formation of solid endothelial cell cords within the superficial parts of the gel. These results suggest that a net positive proteolytic balance is required for capillary lumen formation. A novel perspective is provided on the relationship between extracellular matrix invasion, lumen formation, and net proteolytic balance, thereby reflecting the interplay between **angiogenesis** -modulating cytokines such as bFGF and TGF-beta 1.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Amino Acid Sequence
Base Sequence
Cattle
Cells, Cultured
DNA: GE, genetics
DNA: IP, isolation & purification
Endothelium, Vascular: CY, cytology
Endothelium, Vascular: DE, drug effects
*Endothelium, Vascular: PH, physiology
Enzyme Induction
*Fibroblast Growth Factors: PD, pharmacology
Kinetics
Molecular Sequence Data
*Neovascularization, Pathologic
*Peptide Hydrolases: GE, genetics
Plasminogen Activators: BI, biosynthesis
*Plasminogen Activators: GE, genetics
*Plasminogen Inactivators
*Protein Precursors: GE, genetics
RNA, Messenger: GE, genetics
Restriction Mapping
Tetradecanoylphorbol Acetate: PD, pharmacology
*Transcription, Genetic: DE, drug effects
*Transforming Growth Factors: PD, pharmacology
Urinary Plasminogen Activator: BI, biosynthesis
*Urinary Plasminogen Activator: GE, genetics
Vanadates: PD, pharmacology

CN 0 (Plasminogen Inactivators); 0 (Protein Precursors); 0 (RNA, Messenger); 0 (**Vanadates**); EC 3.4 (Peptide Hydrolases); EC 3.4.21.- (Plasminogen Activators); EC 3.4.21.73 (Urinary Plasminogen Activator)

L10 ANSWER 21 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2002126023 EMBASE
TI Immobilized liposome layers for drug delivery applications: Inhibition of **angiogenesis**.
AU Vermette P.; Meagher L.; Gagnon E.; Griesser H.J.; Doillon C.J.

CS P. Vermette, Department of Chemical Engineering, Intelligent Mat. and Syst. Inst., Universite de Sherbrooke, 2500 Boul. Universite, Sherbrooke, Que. J1K 2R1, Canada. patrick.vermette@courrier.usherb.ca
SO Journal of Controlled Release, (23 Apr 2002) 80/1-3 (179-195).
Refs: 61
ISSN: 0168-3659 CODEN: JCREEC
PUI S 0168-3659(02)00023-8
CY Netherlands
DT Journal; Article
FS 027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
039 Pharmacy
LA English
SL English
TI Immobilized liposome layers for drug delivery applications: Inhibition of **angiogenesis.**
AB Liposomes were immobilized onto the surface of perfluorinated polymer tape samples and tissue culture polystyrene well-plates using a multilayer immobilization strategy. In the first step, a thin interfacial bonding layer with surface aldehyde groups was deposited from a glow discharge struck in acetaldehyde vapour. Polyethylenimine was then covalently bound onto the aldehyde groups by reductive amination, followed by covalent binding of NHS-PEG-biotin molecules onto the surface amine groups by carbodiimide chemistry. Next, NeutrAvidin.RTM. protein molecules were bound onto the PEG-biotin layer. Finally, liposomes containing PEG-biotinylated lipids were docked onto the remaining binding sites of the surface-immobilized NeutrAvidin.RTM. molecules. AFM was used to image surface-bound liposomes and revealed a density well below close packing. The release characteristics of the surface-bound liposomes were measured by the fluorescence intensity changes of carboxyfluorescein upon release. Liposomes filled with sodium orthovanadate were surface immobilized and used in two in vitro **angiogenesis** assays. Marked differences compared to various control samples were observed, demonstrating the utility of drug-filled, surface-bound liposomes for evoking localized, controlled biological host responses proximal to an implanted biomedical device.
CT Medical Descriptors:
***angiogenesis**
immobilization
drug delivery system
covalent bond
amination
vapor
atomic force microscopy
vascular ring
aorta
biotinylation
human
nonhuman
rat
controlled study
human cell
animal tissue
article
priority journal
Drug Descriptors:
*liposome: PR, pharmaceutics
*polystyrene
*propylene

*politef
polymer: PR, pharmaceutics
aldehyde
polyethyleneimine
amine
cyanamide
macrogol: PR, pharmaceutics
vanadate sodium: PR, pharmaceutics
carboxyfluorescein
lipid: PR, pharmaceutics
biotin: PR, pharmaceutics

RN (polystyrene) 9003-53-6; (propylene) 115-07-1; (politef) 9002-84-0, 9039-02-5; (polyethyleneimine) 74913-72-7; (cyanamide) 151-51-9, 420-04-2; (macrogol) 25322-68-3; (**vanadate** sodium) 11105-06-9, 13718-26-8, 13721-39-6; (carboxyfluorescein) 72088-94-9; (lipid) 66455-18-3; (biotin) 58-85-5

L10 ANSWER 22 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 2000141772 EMBASE

TI Tumor necrosis factor employs a protein-tyrosine phosphatase to inhibit activation of KDR and vascular endothelial cell growth factor-induced endothelial cell proliferation.

AU Guo D.-Q.; Wu L.-W.; Dunbar J.D.; Ozes O.N.; Mayo L.D.; Kessler K.M.; Gustin J.A.; Baerwald M.R.; Jaffe E.A.; Warren R.S.; Donner D.B.

CS D.B. Donner, Dept. of Microbiology and Immunology, Indiana University Sch. of Medicine, 1044 W. Walnut St., Indianapolis, IN 46202, United States. ddonner@upui.edu

SO Journal of Biological Chemistry, (14 Apr 2000) 275/15 (11216-11221). Refs: 61
ISSN: 0021-9258 CODEN: JBCHA3

CY United States

DT Journal; Article

FS 029 Clinical Biochemistry

LA English

SL English

AB Vascular endothelial cell growth factor (VEGF) binds to and promotes the activation of one of its receptors, KDR. Once activated, KDR induces the tyrosine phosphorylation of cytoplasmic signaling proteins that are important to endothelial cell proliferation. In human umbilical vein endothelial cells (HUVECs), tumor necrosis factor (TNF) inhibits the phosphorylation and activation of KDR. The ability of TNF to diminish VEGF-stimulated KDR activity was impaired by sodium orthovanadate, suggesting that the inhibitory activity of TNF was mediated by a protein-tyrosine phosphatase. KDR-initiated responses specifically associated with endothelial cell proliferation, mitogen-activated protein kinase activation and DNA synthesis, were also inhibited by TNF, and this was reversed by sodium orthovanadate. Stimulation of HUVECs with TNF induced association of the SHP-1 protein-tyrosine phosphatase with KDR, identifying this phosphatase as a candidate negative regulator of VEGF signal transduction. Heterologous receptor inactivation mediated by a protein-tyrosine phosphatase provides insight into how TNF may inhibit endothelial cell proliferative responses and modulate **angiogenesis** in pathological settings.

CT Medical Descriptors:
*endothelium cell
cell proliferation
DNA synthesis
phosphorylation
signal transduction

immunoprecipitation
immunoblotting
human
controlled study
human cell
article
priority journal
Drug Descriptors:
*tumor necrosis factor
*protein tyrosine phosphatase: EC, endogenous compound
*vasculotropin
receptor: EC, endogenous compound
vanadate sodium
mitogen activated protein kinase: EC, endogenous compound
DNA: EC, endogenous compound

RN (protein tyrosine phosphatase) 79747-53-8, 97162-86-2; (vasculotropin) 127464-60-2; (**vanadate** sodium) 11105-06-9, 13718-26-8, 13721-39-6; (mitogen activated protein kinase) 142243-02-5; (DNA) 9007-49-2

L10 ANSWER 23 OF 23 CANCERLIT
AN 96625810 CANCERLIT
DN 96625810
TI Calcium regulation in cytoskeletal organization during human endothelial cell (HUVEC) spreading (Meeting abstract).
AU Masiero L; Alessandro R; Kohn E C
CS Pathol. Lab., NCI, Bethesda, MD 20892.
SO Proc Annu Meet Am Assoc Cancer Res, (1996). Vol. 37, pp. A327.
ISSN: 0197-016X.
DT (MEETING ABSTRACTS)
FS ICDB
LA English
EM 199606
AB A role for the actin cytoskeleton has been implicated in many cellular functions important in **angiogenesis**, tumor invasion and metastasis. Precise temporal and spatial control of actin filament organization is essential for these activities. We have analyzed early changes in the dynamic reorganization of actin filaments during spreading of serum-starved HUVECs on type IV collagen (cIV) using rhodamine-phalloidin. HUVEC attachment to cIV occurred within the first 15 min and spreading was completed by 90 min. Exposure to 3 uM BAPTA, an intracellular calcium chelator, only during attachment caused an irregular cell shape and loss of adherence to cIV. The same effect was observed with 10 uM CAI, an agent that selectively inhibits calcium uptake and secondarily inhibits calcium-dependent signaling pathways. Exposure of HUVEC to 0.5 uM thapsigargin, a SERCA calcium pump blocker that causes an initial rise in intracellular calcium concentration, induced a rapid and extensive assembly of actin stress fibers accompanied by an increase in polymerized actin at the plasma membrane. The same effect was observed with 1 uM **vanadate**, an inhibitor of phosphotyrosine-specific phosphatases. Prevention of actin stress fiber formation and HUVEC spreading was the predominant phenotype when cells were exposed to the combination of **vanadate** or thapsigargin with CAI. These results indicate that available calcium is necessary for both attachment and spreading of HUVEC and decrease of calcium influx prevents cytoskeletal rearrangement.

=>

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FILE 'CANCERLIT' ENTERED AT 20:44:17 ON 24 JUN 2002

=> s (vanad? and (neovascular? or angiogenic or antiangiogenic)) not l7
L13 17 (VANAD? AND (NEOVASCULAR? OR ANGIOGENIC OR ANTIANGIOGENIC)) NOT L7

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14 9 DUP REM L13 (8 DUPLICATES REMOVED)

=> d 1-9 bib hit

L14 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
AN 2001:693350 CAPLUS
DN 135:262216
TI Tumor-specific peptide motifs for endothelium-specific targeting
IN Wong, Michael K.; Modzelewski, Ruth A.; Brown, Charles Komen; Johnson, Candace S.; Trump, Donald L.
PA University of Pittsburgh, USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001068679	A2	20010920	WO 2001-US8385	20010316
	WO 2001068679	A3	20020530		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	US 2002058615	A1	20020516	US 2001-810700	20010316
PRAI	US 2000-189793P	P	20000316		

AB Peptide motifs which define specificity of tumor-derived endothelial cells are disclosed. These peptides possess a charge motif of pos.-pos.-hydrophobic which is important in detg. the specificity of binding to tumor-derived endothelium. The specific mol. peptide motifs will facilitate diverse therapeutic and diagnostic applications including: anti-**angiogenic** therapies to be used alone or in conjunction with std. therapies; imaging tools for both detection of very small

metastases that are undetectable by current techniques; for monitoring tumor response; for targeting and directing chemotherapy drugs to the tumor; for treatment of chronic inflammatory diseases such as rheumatoid arthritis and psoriasis, for treating some forms of blindness; as well as other diagnostic and therapeutic applications.

IT 10043-66-0, iodine 131, biological studies 10098-91-6, yttrium 90, biological studies 14119-09-6, gallium 67, biological studies 14133-76-7, technetium 99, biological studies 14158-31-7, iodine 125, biological studies 14378-26-8, rhenium 188, biological studies 14701-22-5, nickel II, biological studies 14913-52-1, neodymium +3, biological studies 14998-63-1, rhenium 186, biological studies 15121-26-3, **vanadium** +2, biological studies 15158-11-9, copper II, biological studies 15438-31-0, biological studies 15715-08-9, iodine 123, biological studies 15750-15-9, indium 111, biological studies 15755-39-2, astatine 211, biological studies 15757-86-5, copper 67, biological studies 16065-83-1, chromium III, biological studies 16397-91-4, manganese II, biological studies 18472-30-5, erbium +3, biological studies 18923-27-8, Ytterbium +3, biological studies 20074-52-6, biological studies 22541-17-9, samarium +3, biological studies 22541-19-1, gadolinium III, biological studies 22541-20-4, terbium +3, biological studies 22541-21-5, dysprosium +3, biological studies 22541-22-6, holmium +3, biological studies 22541-53-3, biological studies
RL: ARU (Analytical role, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(tumor-specific peptide motifs for endothelium-specific targeting)

L14 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2001:229074 CAPLUS
DN 134:249233
TI Nuclease inhibitor cocktail for microbiological procedures and kits
IN Winkler, Matthew W.; Kudlicki, W. Antoni; Pasloske, Brittan L.
PA Ambion, Inc., USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001021830	A1	20010329	WO 2000-US26485	20000925
	W: JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRAI	US 1999-155874P	P	19990924		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Angiogenic** factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(nuclease inhibitor cocktail for microbiol. procedures and kits)

IT **Vanadyl** complexes
RL: ARG (Analytical reagent use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); NUU (Other use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleoside, as nuclease inhibitors; nuclease inhibitor cocktail for

microbiol. procedures and kits)

IT Nucleosides, biological studies
RL: ARG (Analytical reagent use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); NUU (Other use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**vanadyl** complexes, as nuclease inhibitors; nuclease inhibitor cocktail for microbiol. procedures and kits)

L14 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
AN 1997:803799 CAPLUS
DN 128:66489
TI Compositions and methods for treating or preventing diseases of body passageways
IN Hunter, William L.; Machan, Lindsay S.
PA Angiotech Pharmaceuticals, Inc., Can.; University of British Columbia; Hunter, William L.; Machan, Lindsay S.
SO PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9745105	A1	19971204	WO 1997-CA345	19970526
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9727604	A1	19980105	AU 1997-27604	19970526
	AU 737078	B2	20010809		
	EP 914102	A1	19990512	EP 1997-921563	19970526
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1219872	A	19990616	CN 1997-194908	19970526
	BR 9710682	A	19990817	BR 1997-10682	19970526
	JP 2000511161	T2	20000829	JP 1997-541313	19970526
	NO 9805463	A	19990121	NO 1998-5463	19981123
	KR 2000015944	A	20000315	KR 1998-709500	19981124
	US 2002052404	A1	20020502	US 2001-933652	20010820
PRAI	US 1996-653207	A	19960524		
	WO 1997-CA345	W	19970526		

AB The present invention provides methods for treating or preventing diseases assocd. with body passageways, comprising the step of delivering to an external portion of the body passageway a therapeutic agent. Representative examples of therapeutic agents include anti-**angiogenic** factors, anti-proliferative agents, anti-inflammatory agents, and antibiotics. Pastes and nanosprays contg. polycaprolactone were prepd.

IT **Angiogenic** factors
Angiogenic factors
Growth inhibitors, animal
Growth inhibitors, animal
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**angiogenic** growth-inhibiting factors; compns. for treating

or preventing diseases of body passageways)

IT 59-05-2, Methotrexate 145-63-1, Suramin 7440-62-2D, **Vanadium**, compds., biological studies 7689-03-4, Camptothecin 9003-01-4D, derivs. 24980-41-4, Polycaprolactone 25189-55-3, Poly(N-isopropylacrylamide) 25248-42-4, Polycaprolactone 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 34346-01-5, Glycolic acid-lactic acid copolymer
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. for treating or preventing diseases of body passageways)

L14 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 1996:649649 CAPLUS
DN 125:293026
TI Induction of E-selectin for targeting therapeutic agents to disease-associated vascular endothelial cells
IN Hallahan, Dennis E.; Weichselbaum, Ralph R.
PA Arch Development Corporation, USA
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9625947	A2	19960829	WO 1996-US2796	19960221
	WO 9625947	A3	19970123		
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5962424	A	19991005	US 1995-392541	19950221
	AU 9651782	A1	19960911	AU 1996-51782	19960221
PRAI	US 1995-392541		19950221		
	WO 1996-US2796		19960221		

IT Blood vessel, disease
(**neovascularization**, E-selectin induction for targeting therapeutic agent to disease vasculature endothelial cell)

IT 7429-91-6, Dysprosium, biological studies 7439-89-6, Iron, biological studies 7439-96-5, Manganese, biological studies 7440-00-8, Neodymium, biological studies 7440-02-0, Nickel, biological studies 7440-14-4, Radium, biological studies 7440-19-9, Samarium, biological studies 7440-27-9, Terbium, biological studies 7440-47-3, Chromium, biological studies 7440-48-4, Cobalt, biological studies 7440-50-8, Copper, biological studies 7440-52-0, Erbium, biological studies 7440-54-2, Gadolinium, biological studies 7440-60-0, Holmium, biological studies 7440-62-2, **Vanadium**, biological studies 7440-64-4, Ytterbium, biological studies 10043-49-9, Gold-198, biological studies 10043-66-0, Iodine-131, biological studies 10045-97-3, Cesium-137, biological studies 10198-40-0, Cobalt-60, biological studies 14119-09-6, Gallium-67, biological studies 14158-31-7, Iodine-125, biological studies 14378-26-8, Rhenium-188, biological studies 14596-37-3, Phosphorus-32, biological studies 14694-69-0, Iridium-192, biological studies 14998-63-1, Rhenium-186, biological studies 15715-08-9, Iodine-123, biological studies 15750-15-9, Indium-111, biological studies 15755-39-2, Astatine-211, biological studies

15757-86-5, Copper-67, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostic; E-selectin induction for targeting therapeutic agent to disease vasculature endothelial cell)

L14 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
AN 1996:102119 CAPLUS
DN 124:171500
TI Protein tyrosine phosphatase regulation of endothelial cell apoptosis and differentiation
AU Yang, Chunlin; Chang, Joan; Gorospe, Myriam; Passaniti, Antonino
CS Lab. Biol. Chem., Gerontology Res. Center, National Inst. AGing, Baltimore, MD, 21224, USA
SO Cell Growth Differ. (1996), 7(2), 161-71
CODEN: CGDIE7; ISSN: 1044-9523
DT Journal
LA English
AB Apoptosis, or programmed cell death, occurs during development and may also be an important factor in many diseases. However, little is known about the signal transduction pathways regulating apoptosis. Here, the loss of endothelial cell-substrate attachment and apoptosis after removal of growth factors was assocd. with dephosphorylation of Tyr residues at the cell periphery. Dephosphorylation of total cellular proteins accompanied apoptosis and was reduced by orthovanadate (Vi), an inhibitor of phosphoprotein tyrosine phosphatases. Vi blocked the fragmentation of nuclear DNA, inhibited DNA laddering, and suppressed the expression of TRPM-2, an apoptosis-assocd. gene. The tyrosine phosphorylation levels of FAK125, erk1 (mitogen-activated kinase kinase), and cdc-2 were reduced during apoptosis. FAK125 dephosphorylation was inhibited by Vi, but premature activation (Tyr dephosphorylation) of cdc-2 was not. Vi was as effective as basic fibroblast growth factor in activating erk1 without increasing cell proliferation and in preventing the apoptosis of endothelial cells after treatment with tumor necrosis factor .alpha.. Endothelial cell differentiation on extracellular matrix (Matrigel) was also stimulated by Vi in the absence of basic fibroblast growth factor without affecting growth arrest and inhibition of DNA synthesis. Expression of the cyclin-dependent kinase inhibitor, p21 (Waf1/Cip1/Sdi1), was down-regulated during the early stages of differentiation, remained low for at least 6 h as differentiation proceeded, and increased upon completion of differentiation. Cells that failed to down-regulate p21 mRNA on Matrigel in the absence of **angiogenic** factors underwent apoptosis. These results suggest that phosphoprotein tyrosine phosphatases are actively involved in signal transduction during apoptosis and may regulate p21 expression to inhibit endothelial cell differentiation.
ST endothelial cell apoptosis regulation phosphoprotein phosphatase; differentiation endothelial cell regulation phosphoprotein phosphatase; **vanadate** endothelial cell apoptosis differentiation

L14 ANSWER 6 OF 9 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 95307363 EMBASE
DN 1995307363
TI Changes associated with tyrosine phosphorylation during short-term hypoxia in retinal microvascular endothelial cells in vitro.
AU Koroma B.M.; De Juan Jr. E.
CS Wilmer Eye Institute, Johns Hopkins Univ. School of Med., 600 N. Wolfe Street,Baltimore, MD 21287-9277, United States
SO Journal of Cellular Biochemistry, (1995) 59/1 (123-132).
ISSN: 0730-2312 CODEN: JCEBD5

CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
012 Ophthalmology
029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
AB The occlusion of capillary vessels results in low oxygen tension in adjacent tissues which triggers a signaling cascade that culminates in **neovascularization**. Using bovine retinal capillary endothelial cells (BRCEC), we investigated the effects of short-term hypoxia on DNA synthesis, phosphotyrosine induction, changes in the expression of basic fibroblast growth factor receptor (bFGFR), protein kinase C (PKC.alpha.), heat shock protein 70 (HSP70), and SH2-containing protein (SHC). The effect of protein tyrosine kinase (PTK) and phosphatase inhibitors on hypoxia-induced phosphotyrosine was also studied. Capillary endothelial cells cultured in standard normoxic (pO2 = 20%) conditions were quiesced in low serum containing medium and then exposed to low oxygen tension or hypoxia (pO2 = 3%) in humidified, 5% CO2, 37.degree.C, tissue culture chambers, on a time-course of up to 24 h. DNA synthesis was potentiated by hypoxia in a time-dependent manner. This response positively correlated with the cumulative induction of phosphotyrosine and the downregulation of bFGFR (M(r) .apprx. 85, kDa). Protein tyrosine kinase inhibitors, herbimycin-A, and methyl 2,5-dihydroxycinnamate, unlike genistein, markedly blocked hypoxia-induced phosphotyrosine. Prolonged exposure of cells to phosphatase inhibitor, sodium orthovanadate, also blocked hypoxia-induced phosphotyrosine. The expression of HSP70, PKC.alpha., and SHC were not markedly altered by hypoxia. Taken together, these data suggest that short-term hypoxia activates endothelial cell proliferation in part via tyrosine phosphorylation of cellular proteins and changes in the expression of the FGF receptor. Thus, endothelial cell mitogenesis and **neovascularization** associated with low oxygen tension may be controlled by abrogating signaling pathways mediated by protein tyrosine kinase and phosphatases.
CT Medical Descriptors:
*cell hypoxia
*retina cell
animal cell
animal tissue
article
capillary endothelium
cattle
cell proliferation
controlled study
dna synthesis
microvasculature
nonhuman
priority journal
protein phosphorylation
retina neovascularization
Drug Descriptors:
fibroblast growth factor receptor
*basic fibroblast growth factor: EC, endogenous compound
*heat shock protein: EC, endogenous compound
*protein kinase c: EC, endogenous compound
2,5 dihydroxycinnamic acid methyl ester: PD, pharmacology
genistein: PD, pharmacology
herbimycin a: PD, pharmacology

protein kinase inhibitor: PD, pharmacology
vanadate sodium: PD, pharmacology
RN (basic fibroblast growth factor) 106096-93-9; (protein kinase c) 141436-78-4; (genistein) 446-72-0; (herbimycin a) 70563-58-5; (**vanadate** sodium) 11105-06-9, 13718-26-8, 13721-39-6

L14 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
AN 1994:477128 CAPLUS
DN 121:77128
TI Role of glutamine-117 in the ribonucleolytic activity of human angiogenin
AU Russo, Nello; Shapiro, Robert; Acharya, K. Ravi; Riordan, James F.; Vallee, Bert L.
CS Cent. Biochem. Biophys. Sci., Harvard Med. Sch., Boston, MA, 02115, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1994), 91(8), 2920-4
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB The crystal structure of human angiogenin reveals that the site that corresponds to the pyrimidine binding site of RNase A is obstructed by Gln-117. Mutation of this residue to Ala and Gly is here found to increase activity 11- to 18-fold and 21- to 30-fold, resp., toward dinucleotide, polynucleotide, and cyclic nucleotide substrates, but without changing specificity. The enhanced activity of Q117G toward CpA is due to a 5-fold decrease in Km and a 6-fold increase in kcat. Its Ki value for 2'-CMP is 5-fold lower than that of native angiogenin, whereas its Ki value for 5'-AMP is unchanged. It has been reported previously that mutating Asp-116 to Ala increases activity 15-fold. The double mutant D116A/Q117A is shown to be only slightly more active than each individual mutant. The present results demonstrate that Gln-117 impedes the ribonucleolytic activity of angiogenin, as predicted by x-ray crystallog. Moreover, they suggest that prior to or during catalysis angiogenin must undergo a conformational change to reorient the C-terminal segment that contains this residue, and that a similar reorganization is required for the mutants as well. This view is supported by mol. modeling of an angiogenin-uridine **vanadate** complex. These in vitro findings have implications for the **angiogenic** activity of angiogenin in vivo.
IT Animal growth regulators
RL: BIOL (Biological study)
(**angiogenic** factors, glutamine-117 in ribonucleolytic activity of, of human)

L14 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 1993:656537 CAPLUS
DN 119:256537
TI Diagnostic and/or therapeutic immunoconjugates targeted to **neovascular** endothelial cells
IN Thorpe, Philip E.; Burrows, Francis J.
PA University of Texas System, USA; Imperial Cancer Research Technology
SO PCT Int. Appl., 171 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 9

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9317715	A1	19930916	WO 1993-US1956	19930305

W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK,

UA, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG

	AU 9337378	A1	19931005	AU 1993-37378	19930305
	EP 627940	A1	19941214	EP 1993-906289	19930305
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	US 6004554	A	19991221	US 1994-295868	19941202
PRAI	US 1992-846349	A2	19920305		
	WO 1993-US1956	A	19930305		

TI Diagnostic and/or therapeutic immunoconjugates targeted to **neovascular** endothelial cells

IT 67-99-2D, conjugates with antibody 1406-72-0D, Restrictocin, conjugates with antibodies 1407-48-3D, .alpha.-Sarcin, conjugates with antibody 4375-07-9D, Epipodophyllotoxin, conjugates with antibodies 7429-91-6D, Dysprosium, conjugates with antibodies 7439-89-6D, Iron, conjugates with antibodies 7439-96-5D, Manganese, conjugates with antibodies 7440-00-8D, Neodymium, conjugates with antibodies 7440-02-0D, Nickel, conjugates with antibodies 7440-19-9D, Samarium, conjugates with antibodies 7440-27-9D, Terbium, conjugates with antibodies 7440-47-3D, Chromium, conjugates with antibodies 7440-48-4D, Cobalt, conjugates with antibodies 7440-50-8D, Copper, conjugates with antibodies 7440-52-0D, Erbium, conjugates with antibodies 7440-54-2D, Gadolinium, conjugates with antibodies 7440-60-0D, Holmium, conjugates with antibodies 7440-62-2D, **Vanadium**, conjugates with antibodies 7440-64-4D, Ytterbium, conjugates with antibodies 9001-99-4D, Ribonuclease, conjugates with antibodies 10043-66-0D, Iodine131, conjugates with antibodies 10098-91-6D, Yttrium90, conjugates with antibodies 14119-09-6D, conjugates with antibodies 14133-76-7D, conjugates with antibodies 14158-31-7D, Iodine125, conjugates with antibodies 14378-26-8D, Rhenium188, conjugates with antibodies 14998-63-1D, Rhenium186, conjugates with antibodies 15715-08-9D, conjugates with antibodies 15750-15-9D, Indium111, conjugates with antibodies 15755-39-2D, Astatine211, conjugates with antibodies 15757-86-5D, Copper67, conjugates with antibodies
RL: BIOL (Biological study)
(to blood vessel endothelium, for tumor diagnosis and treatment)

L14 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
AN 1991:445555 CAPLUS
DN 115:45555
TI Morphological behavior of cultured bovine adrenal medulla capillary endothelial cells
AU Furuya, S.; Edwards, C.; Ornberg, R.
CS Natl. Inst. Physiol. Sci., Okazaki, 444, Japan
SO Tissue Cell (1990), 22(5), 615-28
CODEN: TICEBI; ISSN: 0040-8166
DT Journal
LA English
AB Bovine adrenal medulla capillary endothelial cells were isolated and cloned, and their morphol. behaviors in vitro were examd. In the culture of primary or early passage, one type of colony formed intracellular lumina both on the dish and in the three dimensional collagen gel. Another type proliferated well and showed morphol. ranging from slender-shape to cobblestone shape, and were easily cloned. Cloned cells which showed slender-shapes formed tubular network on plastic dish after addn. of PMA, OAG or **vanadate**, and these cells also formed multicellular tubules in the three dimensional collagen gel. However, the formation of diaphragmed fenestrae by these slender-shape clones was rare. One clone which showed cobblestone shape formed diaphragmed fenestrae,

when cultured on collagen gel for more than one month. Isolated colonies or clones showed heterogeneity of cell shape, **angiogenic** behaviors and fenestrae formation.